Date - 4/30/07 - 4:40pm

Faxed to - 571-273-9078

RECEIVED
CENTRAL FAX CENTER
APR 3 0 2007

For Helen Mei-Ping Chui - Examiner

Application No. 10/749,314 - Art Unit 1609
Applicant – McLane, Mchael W.

Rule below that applies in place of 35 USC / 102(b) for Claims

35 U.S.C. 135 Interferences.

Also, enclosed, please find more documents that clearly show that Dr. Malcolm Carruthers is not the inventor of Danazol for hypogonadism in males as he claims in his patent application – US 2002/0115,648 on August 22, 2002

Dr. Carruthers became aware of low dose Danazol as treatment for hypogonadism in the male human for the first time when he arrived for Zeneca's discussions in Dec. 1993. In those discussions, it was clearly represented by myself and Zeneca's management that I had invented Danazol as a new and novel treatment for hypogonadism.

Signed –

M.W. McLane 4/30/07 4:40 pm

Michael W. McLane

CTC received 5/2/07

2 of 6

ZENECA Pharmaceuticals Group

RECEIVED
CENTRAL FAX CENTER
APR 3 0 2007

Date: January 3, 1994

To: Ralph Giles **cc:** Mike McLane
Larry Steranka

From: Ron Burch

Subject: **Oral hormonal replacement in the male**

I found the proposal by McLane to be scientifically interesting. There would likely be a market for an agent that could compete with testosterone for its plasma binding site, increasing free testosterone concentration and making it available to bind to its cytosolic receptors. In most cases, binding to plasma proteins does not actually make a drug less available to physiological receptors since those generally have quite high affinity compared to the plasma protein sites. However, it is well-documented that the sex steroid binding globulin has a similar affinity as the cytosolic receptor and an enormous concentration compared to the cytosolic receptor, making it the pool to which testosterone binds. Clearly there are recognition differences which make it feasible to design molecules that would bind only to the globulin.

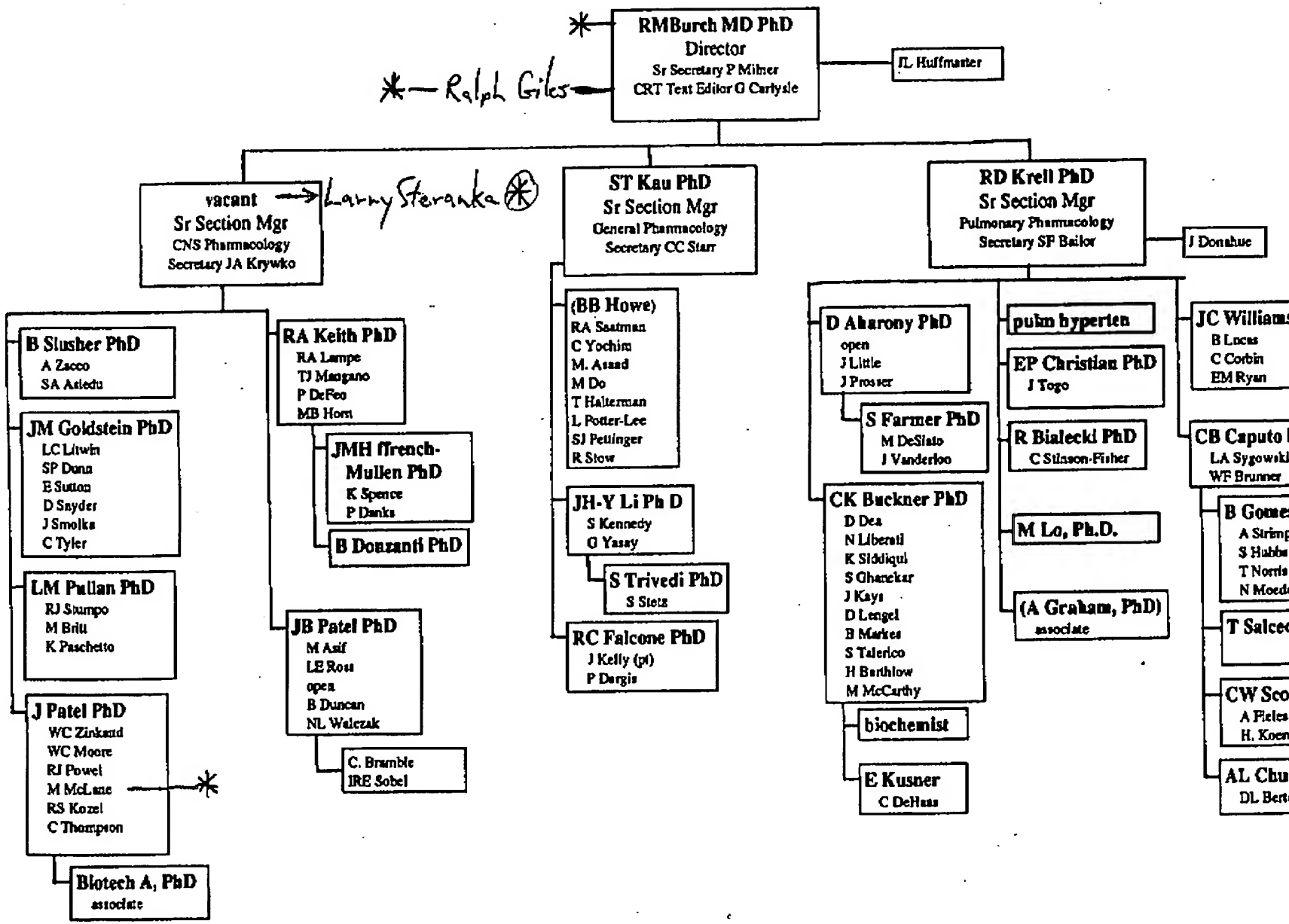
The only problems I have with the proposal are practical ones. Use patents are fine in the U.S. if they can be gotten (I would think that danazol and norgestrel would be difficult to get past the hurdle as obvious, but I am not a patent attorney). Unfortunately, outside the U.S. use patents are not particularly useful. Also, as Caruthers noted, testosterone undecanoate and another agent are orally effective in man. Also, given the tightness of money and richness of pipeline, I would doubt that anyone in the NPRDC would give even a glance at a known compound, sold by someone else for related purposes, with a tenuous use patent, with the knowledge that other agents are orally active and do work in man.

I have no interest in pursuing this opportunity. If there is further interest on Mike's part, then clearly the project falls within VIM's "remit," and Barry Furr certainly is the world's foremost drug finder (rather than hunter) in the area of male and female sex steroids.

Dr. Malcolm Carruthers visited and gave his expert opinion concerning my invention with Danazol in Dec. 1993.

JH ASTHMA & ALLERGY Fax:4105502090 Apr 30 2007 17:49 P.03

Zeneca Management - 1993



PAGE 3/6 * RCVD AT 4/30/2007 4:43:52 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-6/2 * DNIS:2739078 * CSID:4105502090 * DURATION (mm-ss):01-10

Carruthers, Malcolm ~~1-011-44-71-738-5651~~

Hormonal Healthcare Center

Work - Desk →

~~Home~~? 1-011-44-71-224-0478

935-1811 Hippocrates -

American # 4848
JFK → Phila.
10:10 → 11:20

My Rolodex record of Carruthers, Malcolm (1993)

— Noting his American Airlines flight #4848 from JFK into Phila. Airport - (Dec. 1993) in order to speak with Zeneca management about my Danazol invention. He gave a formal seminar on "Andropause" and then answered questions from Zeneca management about my Danazol invention and its marketability.

M. W. McLane

Michael W. McLane

INTERNAL MEMORANDUM

ZENECA Pharmaceuticals Group
Biomedical Research Department
Telephone (302) 886-5943

DATE: 15-Nov-1993 03:16pm EST

TO: Ralph Giles

FROM: Michael W. McLane

CC: Andrew Shaw

SUBJECT: Use-Patent Feasibility for Danazol (oral male HRT)

Zeneca Pharmaceutical Group is in a strong position to obtain new use-patents on each of the proposed compounds (i.e. Danazol, 2-methoxyestradiol, and Norgestrel).

According to the U.S. Patent Office, new use-patents are awarded upon meeting three criteria. They are:

1. Nonobviousness
2. Novel use
3. Effectiveness

I. Seemingly, the most difficult criteria will be demonstrating the "non-obviousness" of our inventions since they were deduced solely from published pharmacological literature. Here, however, we should invoke the Patent Office's "secondary rule of evidence for non-obviousness". This rule states that if a use-patent relies on previously published data the invention could still be non-obvious if no other expert in the field has as yet proposed said invention, having had similar access to the published data for a reasonable period of time.

The above fits our situation.

Specifically, the new use-patent for Danazol stems from an insightful reinterpretation of published data that is 8-20 years old. For instance:

1. Danazol's "impedent" androgenicity in male rats was published in 1971. (this early misinterpretation of Danazol's mechanism of action led pharmacologists in the field to discount this drug's androgenic potential)

2. Danazol's true mechanism of action as a competitive displacer of testosterone from sex hormone binding globulin (SHBG) was published in 1981.

3. The primary importance of SHBG in determining free testosterone levels in the male body was published in 1985.

The "non-obvious" integration of these long published

observations with more recent findings forms the basis for our new use proposal for Danazol.

II. The second criteria of "novel use" is satisfied in that Danazol has never before been developed as a commercial hormonal replacement therapy (HRT). Our patent is for a new use of a generic drug that would even target a different patient population than is currently served. Also, different formulations distinct from the current product would be required. Unique formulations (i.e. 1 and 5 mg. doses vs. 50 and 100 mg) will effectively prevent "unintentional" competition from generic Danazol sources.

III. The last criteria, "effectiveness", can be sufficiently supported by a discussion of current scientific understanding of testosterone physiology in the aging male.

Immediate pursuit of all three use-patents is warranted. When all use-patents are filed at a nominal cost, the company will have protected its interests. The long and more expensive process of obtaining approval of the Danazol use-patent should then begin.